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## ASSESSMENT OF HORMONAL RECEPTORS AND HER2 BEFORE AND AFTER NEOADJUVANT CHEMOTHERAPY IN BREAST CANCER

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**Introduction and objectives:** Neoadjuvant chemotherapy (NACT) has traditionally been the standard management for inflammatory and locally advanced cancer. Testing the tumor core biopsy samples is a prerequisite for selecting patients into the neoadjuvant route. Few studies to date have examined the effect of neoadjuvant chemotherapy on the hormone receptor status of primary breast carcinomas with somewhat conflicting results. Due to this contradictory results, there has been inconsistency in practice worldwide with uncertainty as to whether testing on residual carcinoma is warranted and if treatment options should be modified based on the final molecular profile of the tumor. In our retrospective study, we compared the immunohistochemical expression of HR and HER2 in core biopsy samples with that in the surgical excision specimens to ascertain concordance and discordance rates in breast cancer patients with NAC

**Patients and Methods:** We retrospectively collected data from the records of patients with locally advanced breast cancer who had undergone preoperative biopsy and subsequent surgical resection after neoadjuvant therapy at Ain Shams University hospitals in 2016 and 2017. 40 patients were included. We evaluated the concordance rates for ER, PR, and HER2 expression between the preoperative biopsy and final specimens after neoadjuvant therapy.

**Results:** The ER status changed in only 4 patients; from ER positive to ER negative in 3 patients, and from negative to positive in only 1 patient, while it remained unchanged in the rest 36 patients. PR status changed in only 5 patients from positive to negative in 4 patients and from negative to positive in 1 patient HER2 status changed in only 4 patients. HER2 positive to HER2 negative in 1 patient and from HER2 negative to HER2 positive in only 3 patients, while it remained unchanged in the rest 36 patients

**Conclusion:** This study demonstrates no significant difference in ER, PR or HER2 expression by IHC in pretreatment and post-treatment primary breast carcinomas. However, there were other studies with statistically significant decrease in PR expression by IHC following neoadjuvant chemotherapy, the cause and clinical significance of which require further investigation.

## MODIFIED ROUND BLOCK ONCOPLASTIC TECHNIQUE FOR CANCER BREAST, DOES IT FIT FOR ALL PATIENTS?

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**Introduction:** Round block technique (RBT) is often utilized in breast-conserving surgery, but has problems of late-onset scar widening and changes in the shape or the position of the areola. We have modified RBT (MRBT) to resolve those problems.

**Purpose:** This research was conducted to study the feasibility, safety and cosmetic results of MRBT for cancer breast in all quadrant of the breast.

**Patients and Methods:** Forty breast cancer patients were treated with MRBT. A circumferential incision was made without excision of the periareolar skin, and subcutaneous dissection was extended to the entire breast. The wound could be widened and moved onto the distant tumor by application of a wound retractor. Partial mastectomy was then performed under direct vision. The wound was easily closed without tension.

**Results:** The median distance between the nipple and the tumor was 5.2 cm, and the median areolar size was 2.8 cm. Cosmetic results were satisfactory with minimal scar formation. There were neither subsequent changes in the shape nor the position of the areola. MRBT is a useful oncoplastic technique in patients with small areolae, and/or when the tumor location is distant from the nipple.

**Conclusion:** MRBT is a relatively newer technique used for all quadrant located breast tumors associated with wider surgical exposure, favorable cosmetic results and high degree of patient satisfaction.

**Keywords:** Modified round block technique, oncoplastic, cancer breast.

## EVALUATION OF HEALTH-RELATED QUALITY OF LIFE IN CANCER PATIENTS RECEIVING CHEMOTHERAPY

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**Introduction and Objectives:** Cancer is considered as the second leading cause of death worldwide, so improving health related quality of life (HRQOL) of patients is mandatory. It is important to have a clinically useful HRQOL assessment and to evaluate HRQOL among cancer patients receiving chemotherapy.

**Material and Methods:** This cross sectional study included 190 cancer patients who have been received chemotherapy at the day care clinics in Nasser Institute Cancer Center (NICC). To address our subject, we analyzed HRQOL, as measured with the Functional Assessment of Cancer Therapy-General questionnaire (FACT-G), Arabic Version 4, and depicted the complex relations among physical, psychological, social, and cultural factors.

**Results:** From 190 cancer patients [aged from 23 to 81 years (50.63±11.79)] 153 patients (80.53%) were females. FACT-G total score ranged from 21.2 to 87 (63.24±12.74) which is considered relatively poor being the physical and functional domains were more affected. HRQOL of the study group was not affected by gender, employment status, education level, smoking habits or marital status while it was negatively correlated with age, time since diagnosis of cancer, and disease stage. Patients' HRQOL shown to be affected by the presence of many variables like low performance status as evaluated by Eastern Cooperative Oncology Group (ECOG) scale, associated comorbidities, exposure to radiotherapy, history of surgery, and absence of menstrual status in female patients. A positive correlation was found between HRQOL and higher body mass index (BMI), and it was observed that the HRQOL of patients with higher perceived financial status was better.

**Conclusions:** The HRQOL of cancer patients who were receiving chemotherapy at NICC in our study tended to be lower than the norms of the healthy people. Preplanned health programs should be designed for cancer patients to support early disease diagnosis, optimizing treatment choices, controlling of associated comorbidities, improving patients' performance status as well as working on improving health insurance coverage.

## LONG NON-CODING RNA NEAT1 PROMOTES TUMORIGENESIS IN HIGH GRADE SEROUS OVARIAN CANCER AND IS REGULATED BY LIN28B

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**Objective:** Aberrant expression of long noncoding RNAs (lncRNAs) in specific cancers has frequently been reported, including those of high grade serous ovarian cancer (HGSOC). Accumulating evidence demonstrates that lncRNAs play important roles in regulating gene expression and are involved in various pathological processes. The purpose of the present study was to explore the clinical significance and underlying mechanism of a significantly dysregulated lncRNA-NEAT1 in HGSOC.

**Materials and Methods:** NEAT1 was got from the lncRNAs profiling of ovarian cancer in The Cancer Genome Atlas (TCGA) database, its expression level was further verified in 75 HGSOC tissues and 75 normal ovarian tissues collected from cervix cancer surgery patients, as well as ovarian cancer cell lines, and its association with clinical significance were then analysed. CCK-8 assay and colony formation were used to measure cell proliferation. Cell migration then was detected by transwell migration and invasion assay. In order to evaluate the mechanism of NEAT1 in HGSOC, Bioinformatics analysis combined with RIP and Pulldown assay were performed to determine the potential binding protein. RNA and protein expression were measured by qRT-PCR and Western blotting, respectively.

**Results:** Our results showed that NEAT1 expression was significantly up-regulated in cancerous tissues and cell lines compared with normal counterparts. High NEAT1 expression was closely associated with tumor size. Moreover, linc00152 could serve as an independent predictor for overall survival. Further functional experiments demonstrated that knockdown of NEAT1 significantly prohibited the proliferation and invasion of ovarian cancer cells. LIN28B was identified as a direct actor with NEAT1 by bioinformatics analysis, further experiments showed that LIN28B was able to bind NEAT1 and induced NEAT1 expression. Overexpression of LIN28B can stabilize NEAT1. NEAT1 fulfilled its oncogenic functions by a LIN28B-mediated manner.

**Conclusions:** Together, the discovery of our study uncovers the oncogenic role of lncRNA-NEAT1 in HGSOC and the LIN28B/NEAT1 axis which has not yet been reported. These results propose that combinatorial targeting of NEAT1 and LIN28B may represent a unique therapeutic regimen within patients with HGSOC.

## THE EXPRESSION OF MAGE-A10 IN EPITHELIAL OVARIAN NEOPLASMS: AN IMMUNOHISTOCHEMICAL STUDY

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**Introduction:** MAGE-A10 is a member of the cancer/testis (CT) antigen family that shows a restricted pattern of expression in gametogenic tissue and various malignant tumors but silenced in normal tissue. As the most immunogenic member of the family, MAGE-A10 is proposed as a target for cancer immunotherapy. The aim of the study was to investigate the distribution and biological significance of this new CT antigen in epithelial ovarian neoplasms.

**Material and Methods:** This study was conducted on 72 epithelial ovarian neoplasms including 13 benign, 16 borderline and 43 malignant tumors. Histological subtypes of benign and borderline cases included serous, mucinous and Brenner tumors. Malignant cases were segregated into type I and type II epithelial ovarian cancers (EOCs). Type I EOCs included low-grade serous, low-grade endometrioid, mucinous and clear cell carcinomas as well as malignant Brenner. Type II EOCs included high-grade serous and high-grade endometrioid carcinomas. Immunohistochemistry was performed on paraffin-embedded tissue using the polyclonal antibody against MAGE-A10-Carboxyterminal end. Statistical analysis was performed to determine its association with clinicopathological parameters and patients' outcome.

**Results:** MAGE-A10 was expressed in 100% of the studied epithelial ovarian neoplasms with a total score ranging from 2 to 12 and a median of 6. Heterogeneity was discerned in only 14% of EOCs. Its expression showed a highly significant increase from benign to borderline to malignant type I EOCs ($p$=<0.001) which was respected when considering serous and mucinous tumors independently [($p$=0.024 and $p$=0.008) respectively]. No significant difference in its expression was detected between type I and type II EOCs ($p$=0.783). In EOCs, high MAGE-A10 expression was found to be significantly associated with shorter disease/progression-free survival ($p$=0.012) and partial response to chemotherapy ($p$=0.016). MAGE-A10 was significantly correlated with patients' age ($p$=0.039) but not FIGO stage, grade or histological subtype of EOC.

**Conclusions:** MAGE-A10 is possibly implicated in the early steps of ovarian carcinogenesis particularly in type I EOCs. Its elevated expression in EOCs is a probable poor prognostic factor that can adversely affect patient outcome. Lastly, the ubiquitous and non-heterogeneous manner of MAGE-A10 expression highly advocates it as an excellent target for immunotherapy in EOCs.

## FEASIBILITY AND FUNCTIONAL OUTCOME OF LAPAROSCOPIC NERVE SPARING RADICAL HYSTERECTOMY

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**Introduction:** To evaluate the feasibility and the functional outcome of laparoscopic nerve sparing radical hysterectomy (LNSRH) technique in cervical cancer and locally advanced endometrial cancer patients.

**Materials and methods:** From November 2014 to November 2016, patients who underwent laparoscopic type C1 hysterectomy (n=30) and laparoscopic type C2 (n=16) hysterectomy according to Querleu-Morrow classification at the department of Surgical Oncology, Oncology center Mansoura university, Mansoura, Egypt and the department of gynecologic oncology, Catholic University of sacred heart Rome, Italy were prospectively evaluated.

**Results:** 46 patients were included in the study, 30 patients underwent type C1 LNSRH (Group A) and 16 patients underwent type C2 LRH (Group B). The mean age was 49.1±13.1 and 51.2±11.8, median BMI was 26.2(22.9-28.5) and 23.8(21-26.6) respectively for the 2 groups. Group A had 25 patients with cervical cancer with FIGO staging (IB1-IIB) and 5 patients with endometrial cancer FIGO staging (II-IIIC) while all 16 patients of group B were cervical cancer patients with FIGO staging (IB1-IIIB). The mean operative time was 240.1±65.5 in group A and 308.1±83 in group B (P=0.004). No significant statistical difference was found between the 2 groups as regard the median blood loss 100 (50-150) ml in group A and 125 (100-200) ml in group B, the rate of intraoperative complications (10%) in group A and (12.5%) in group B, total number of harvested LN and unplanned conversion to laparotomy rate (P>0.05). The median duration of postoperative catheterization until the PVR urine volume was less than 100 ml was 3.5(3-5) days in group A and 6(4-8.5) days in group B (P=0.002) None of the patients of group A complained of bladder dysfunction symptoms during the follow up period while 3 patients in group B had bladder dysfunction symptoms (P=0.037)

**Conclusions:** Our results support the feasibility of laparoscopic nerve sparing radical hysterectomy technique with better bladder functional symptoms.

## TUMOR-INFILTRATING FOXP3+ REGULATORY T CELLS AND PROGRAMMED CELL DEATH LIGAND (PDL1) EXPRESSION IN EARLY STAGE TRIPLE NEGATIVE BREAST CANCER TREATED WITH NEOADJUVANT CHEMOTHERAPY

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**Introduction:** The effects of neoadjuvant chemotherapy (NAC) on the tumor immune markers remain widely unknown. Several studies have suggested that chemotherapeutic agents may exert their anti-tumor activity by the induction of an anti-tumor immune response directed at tumor cells injured by chemotherapy. This study aimed to assess changes in TILs count, Foxp3+ regulatory T Cells and PD-L1 expression in paired pre-neoadjuvant and post-neoadjuvant chemotherapy specimens in early stages TNBC patients (T1 and T2) and correlated residual cancer TIL counts, Foxp3+ regulatory T Cells and PD-L1 expression and change in these parameters with survival.

**Materials and Methods:** Fifty patients of TNBC patients were enrolled in this study, which had undergone core biopsies for diagnosis. Twenty five cases of them received neoadjuvant chemotherapy while the other 25 were followed up without treatment. TILs count, Foxp3+ regulatory T Cells and PD-L1 immunohistochemical expression were investigated in all cases before NAC and then evaluated in residual masses of the treated 25 cases after surgery. Data on survival and response to the chemotherapy were collected and then statistically analyzed.

**Results:** PDL1 expression was detected in 24% of all studied cases, all them are node positive (P value <0.002); while Foxp3+ expressed in 50% and high TILs in 28% of them. Complete pathological response was achieved in 40% of patients under NAC with high significant difference (P value<0.0001). Pathologic complete response (pCR) to neoadjuvant chemotherapy is associated with high TILs expression (P value <0.02) and absence of Foxp3+cells. PDL1 expression was decreased in post- treatment samples but without significant difference. High TILs count was associated with long survival ($p < 0.05$).

**Conclusions:** PD-L1 is expressed in 24% of TNBCs, so it is considered as a therapeutic target in TNBCs. Neoadjuvant chemotherapy in early stages TNBC is associated with a higher pCR rates which predict better survival. High TIL count is associated with higher pCR rate after neoadjuvant chemotherapy.

## IMPACT OF NEOADJUVANT CHEMOTHERAPY ON SURGICAL TREATMENT OF BREAST CANCER

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**Introduction:** Neoadjuvant chemotherapy is being increasingly used for the treatment of breast cancer. Response to neoadjuvant chemotherapy may convert an inoperable breast cancer to an operable tumor. By downsizing the tumor, neoadjuvant chemotherapy also increases the possibility of breast conserving therapy in larger number of patients.

**Patients and Methods:** Between October 2015 to February 2017, a total of 62 breast cancer patients aged 50 ± 8 years with Stage II and Stage III disease were enrolled in this study. All patients received neoadjuvant chemotherapy in the form of Anthracycline/Taxane based regimen for 6 cycles. Clinical and pathological response were estimated after the completion of the regimen. The molecular type of breast cancer and the response were compared. The response reached and the surgery performed were also compared.

**Results:** 38 patients underwent Breast Conservative surgery and 24 patients underwent Modified Radical Mastectomy. 19 patients reached to complete clinical response, 9 patients were Triple Negative, 4 were Her2 enriched, 2 were Luminal A, 2 were Luminal B1 and 2 were Luminal B2. 18 of them underwent Breast conservative surgeries except for one who missed the placement of a clip or wire so a definite clear safety margins could not be attempted.

**Conclusion:** Neoadjuvant treatment is very effective in downsizing tumors, facilitating breast conservative surgery in 61% of patients enrolled in our study. Better response is expected in hormones negative and HER2 positive cases. Clip application to the tumor has essential role to guide the surgeon to the remaining tumor tissue, thus making BCS possible.

## ROADMAP OF LYMPH NODES SAMPLING IN ENDOMETRIAL CANCER

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**Introduction & Objective:** The aim of this study was to evaluate Para-aortic lymph node metastasis in cases with endometrial cancer and to correlate it with pelvic node metastasis.

**Method:** Retrospective analysis of data from patients' records who had total abdominal hysterectomy and bilateral salpingoophrectomy for endometrial cancer between 2007 till 2013, and the procedure involved pelvic lymphadenectomy and Para-aortic lymphadenectomy or sampling of enlarged lymph nodes. A total of 202 patients who had their surgery at Mansoura University were enrolled in this study.

**Results:** Twenty two patients were found to have metastasis for PANs.

Twenty out of 26 patients with common and/or external iliac positive lymph nodes had shown PAN metastasis. Two out of 176 patients with negative pelvic lymph nodes had shown positive PAN metastasis. Based on these data, common and/or external iliac lymph nodes had 90.9% sensitivity (20/22) and 96.7% specificity (174/180) for detecting PAN metastasis.

**Conclusion:** Para-aortic lymphadenectomy might be avoided by the negativity of pelvic lymph nodes, thereby minimizing post-operative complications.

**Key words:** endometrial cancer, lymphadenectomy

## SELECTIVE CYTOTOXIC EFFECTS ON HUMAN BREAST CARCINOMA OF NEW METHOXYLATED FLAVONOIDS FROM EURYOPS ARABICUS GROWN IN SAUDI ARABIA

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**Introduction & objective:** Cancer is one of the leading causes of death in the world [1,2]. The International Agency for Research on Cancer reported that, more than 7 million people died from cancer in 2008 and it was anticipated that it is going to be more or less triplicate by the year 2030 [3]. The treatment of cancer was recently designed by two major approaches aiming at discovering potent antitumor metabolites; bio-chemical and targeted-based. The former gained a significant attention in the recent two decades, which led to discovery of several antitumor agents The chloroform methanol extract of Euryops arabicus, collected from Saudi provenance, yielded a new kaurane diterpene (1) and seven methoxylated flavones (2e8), two of which are new (2 and 3). Structures of the compounds were elucidated through interpretation of spectral data of NMR, MS and comparison with literature values. All compounds were evaluated for their anti-tumor activities, employing four different cancer cell lines (WI-38, VERO, HepG2 and MCF-7), ABTS free radical scavenging and immune modulatory effects.

**Results:** All metabolites had considerable antioxidant and immune stimulatory effects. All compounds showed anticancer activity with IC50 in range 10e125 mM, whilst 2 and 6 showed significant anti-proliferative activity against HepG2 (IC50 ¼ 20 and 15 mM) and MCF-7 (IC50 ¼ 15 and10 mM), respectively.

**Conclusion:** From the aerial parts of E. arabicus, a new kaurane diterpene;18,19-dihydroxy-kaura-16-en-3-one (1) and two new flavonoids (2and 3) and five known flavonoids (4e8) were obtained. The isolated metabolites showed considerable antioxidant and immune stimulatory effects. Nonetheless, 2 and 6 showed promising antiproliferative effects comparable to positive control 5 fluorouracil (5-FU), which was attributed to S-phase cell cycle arrest.

## ABBREVIATED BREAST MRI PROTOCOLS, THE NEW COMER IN BREAST IMAGING

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**Introduction and Objectives:** Breast MRI has recently become a corner stone in breast imaging particularly with the recent changes in breast cancer management and the introduction of neoadjuvant chemotherapy. However, the traditional protocol takes long time to acquire and to report, hence the value of abbreviated breast protocol as a substitute of the traditional breast MRI for detection of different breast lesions is raising great concern recently.

**Patients and methods:** Retrospective review of 143 breast MRI examinations performed at our institution on a 1.5 T scanner from January 2016 to October 2017 by two radiologists (with 7 and 5 years of experience in breast imaging). Reviewing the abbreviated protocol first (consisting of the first post-contrast subtracted [FAST] and maximum-intensity projection [MIP] images), followed by reviewing the full protocol. Data were collected from each revision separately including the findings and the time of the analysis.

**Results:** Significant reduction of the scan acquisition time was noted when using the abbreviated protocol (about 83% reduction). Detection of lesions on the abbreviated protocol took about 25 seconds in comparison to 15 minutes when reviewing the full protocol. Of the reviewed 143 patients, 15 were malignant and 68 showed benign lesions and 60 showed normal scan. Abbreviated protocol was able to detect all the 15 malignant lesions with a PPV of 100% and 66 out of 68 benign lesions (97.1 %) with negative predictive value of malignancy reaching 100%.

**Conclusion:** The abbreviated protocol, consisting of the first post-contrast subtracted image and MIP images is raising great benefit over the full diagnostic protocol since it shows marked reduction scan time as well as the reading time with nearly equal detection rates of different breast lesions as well as it is considered a good negative scan that can be used in screening of high risk patients.

## PATHOLOGICAL COMPLETE RESPONSE IN OBESE PATIENTS RECEIVING NEOADJUVANT CHEMOTHERAPY FOR BREAST CANCER

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**Introduction:** Obesity is an independent adverse prognostic factor in early breast cancer [1]. Controversy exists regarding the relation between obesity and pathological complete response (PCR) to neoadjuvant chemotherapy (NAC) in breast cancer [2,3]. The aim of this study is to evaluate the relationship between obesity and PCR to NAC in breast cancer patients.

**Material & Methods:** This is a retrospective study conducted at Kasr Al-aini Center of Clinical Oncology and Nuclear medicine (NEMROCK) between January 2011 and December 2015. Of the 3800 patients diagnosed with breast cancer in this period, 269 patients with stage II and III breast cancer who received neoadjuvant chemotherapy were included. Patients were divided into three groups according to BMI as normal/underweight (BMI < 25 kg/m2), overweight (BMI= 25-29.9 kg/m2) and obese (BMI >30 kg/m2).[4]

**Results:** Seventy (26.1%) of the patients were normal/underweight, 88 (32.7%) patients were overweight and 111 (41.2%) patients were obese. There was no significant difference in clinicopathological features between groups. PCR was achieved in 74 (27.5%) of patients in all groups which was higher in normal/underweight (34.2%, n=24/70) when compared to overweight (27.2%, n= 24/88) and obese patients (23.4%, n= 26/111) with considerable trend towards significance (P=0.09 in chi-square test). In a multivariate analysis, obesity was an independent negative predictor of PCR to neoadjuvant chemotherapy compared to normal/underweight patients.

**Conclusion:** obesity significantly affect PCR after adjusting clinically significant factors.

**Keywords:** obesity, breast cancer, PCR

## AXILLARY IRRADIATION IN BREAST CANCER; DOES METICULOUS CONTOURING MAKE A DIFFERANCE?

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**Introduction:** With the current trends toward replacing axillary dissection with radiotherapy, and need for more precise definition for different nodal stations, contouring of axilla becomes a must to ensure safe and adequate dose coverage.

**Aim:** To evaluate the coverage of axillary nodal volumes based on PROCAB guidelines, for cases previously treated with our standard tangential approach.

**Material & Methods:** Computed tomography (CT) images of ten previously treated patients with different anatomical and surgical parameters were selected. For each patient, a new contouring based on PROCAB (PROject on CAncer of the Breast) guidelines were done for each LN station. Adequate dose coverage was assessed for all volumes using our Eclipse version 11 planning system.

**Results:** The mean volumes of axillary levels I, II and III were 33.29 cm3 (range 18.6 – 54.8cm3), 13.27 cm3 (range 9.4–16.8 cm3) and 12.84 cm3 (range 7.9—18.2 cm3), respectively. Dose coverage for 95% of prescribed dose for each axillary LN volumes was assessed separately. Level I and II and III lymph nodes received a mean D95% of 11.6 Gy, 11.9 Gy and 25.8 Gy respectively. Mean dose of 31.3 Gy and 29.08 Gy, and 35.38 Gy respectively.

**Conclusion:** PROCAB guidelines presents a method for standardization of axillary LN delineation. More advanced radiotherapy planning is needed to improve coverage of axilla in post-operative treatment of breast cancer.

**Keywords:** Breast cancer, Radiation therapy, PROCAB guidelines, Axillary lymph node.

## THE RISK OF CHRONIC MYELOID LEUKEMIA IN FEMALE BREAST CANCER PATIENTS; A US POPULATION-BASED STUDY

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**Introduction:** Breast cancer is the most common malignancy affecting females and accounting for 30% of cancer cases in the US in 2017. Ample evidence is accumulating about the risk of second primary malignancies in breast cancer patients. However, no large-scale cohort studies were performed to study the risk of developing a second chronic myeloid leukemia (CML) after breast cancer.

**Methods:** We used the Surveillance Epidemiology and End Results 'SEER' database to review females with breast cancer diagnosed during 1992-2014 were selected and followed for the development of CML after a six-month latency period. We calculated the Observed/Expected (O/E) ratio, to estimate the change of risk of CML following breast cancer diagnosis when compared to the general US population.

**Results:** We included 474,866 females with breast cancer, of which 178 were diagnosed later with CML. The risk of CML increased significantly after breast cancer diagnosis with an O/E of 1.26. When divided according to the latency period between the two diagnoses, the increase was significant within the first five years following breast cancer diagnosis with 84 cases and an O/E of 1.45. After five years of the diagnosis, the risk returned to normal and O/E ratio did not change significantly from the normal general population. Most cases were whites and their risk increased significantly (O/E=1.26). Moreover, 13 cases were Asians or pacific islanders with significantly increased O/E of 1.99. However, the risk among other races did not change. When cases were analyzed according to the stage of breast cancer, the only stage to show a significant increase was regional, with 55 cases and O/E of 1.56. The overall CML risk of localized breast cancer cases did not change, but their risk was significantly higher within the first five years following breast cancer diagnosis (O/E=1.40).

**Conclusions:** Females diagnosed with breast cancer have an increased risk of developing CML, and further studies are required to establish the causes of this increase. Screening programs may help in early detection, and thus decreased mortality and morbidity. Furthermore, studies are needed to determine the benefits of possible interventions to this population.

## BENEFITS OF AEROBIC EXERCISE INTERVENTIONS AMONG BREAST CANCER SURVIVORS: A SYSTEMATIC REVIEW OF RANDOMIZED CONTROLLED TRIALS

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**Background:** Physical exercise might be of great benefit to breast cancer survivors. The purpose of this review is to comprehensively and systematically summarize the effects of aerobic exercise intervention in breast cancer survivors.

**Methods:** We searched PubMed, web of knowledge, Scopus, Cochrane Central, Virtual Health Library and PEDRO for randomized controlled trials (RCTs) that compared the Aerobic Exercise with usual care in BC survivors up to February 2017.

**Results:** Based on our criteria, only 12 studies were eligible to be reviewed. Compared with the usual care, quality of life was significantly improved in aerobic exercise intervention group, especially in the well-being and social well-being subscales of the Functional Assessment of Cancer Therapy. Exercise alleviated the symptoms of depression and anxiety as well. Furthermore, the serum concentration of insulin, insulin-like growth factor-II, and insulin-like growth factor binding protein-1 was significantly reduced among the aerobic exercise intervention group. However, current evidence, showed no significant benefits in terms of weight loss and other inflammatory markers.

**Conclusion:** Our review suggests that aerobic exercise intervention is beneficial to breast cancer survivors. Thus, it should be recommended in their therapeutic regimen.

**Keywords:** Aerobic Exercise, Quality of Life, Breast Cancer Survivors, Physical Activity

## BREAST CANCER RISK IN HCV CIRRHOTIC FEMALE PATIENTS AS ASSESSED BY SONO-MAMMOGRAPHY: AN EGYPTIAN PILOT STUDY

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**Introduction:** HCV shows a high propensity to establish liver cirrhosis and HCC ranking the first in Egypt, whereas breast cancer occupies the second. Cirrhosis shows elevated Estradiol (E2) level, that regulates the breast's fibroglandular tissue (density), increasing the likelihood of breast cancer. The Aim is to assess the relationship between HCV and breast cancer addressing the relations between: E2, Cirrhosis and Breast density.

**Methods and Materials:** This is a pilot study, based on a multidisciplinary counseling including 54 Control cases (Same age group 55-72 y) and another 54 known to be Postmenopausal cirrhotic, Child (A, B, C) with exclusion criteria of receiving estrogen containing drugs/Tamoxifen and those unable to consent. All patients were subjected to: a) Both breasts blinded Mammography and breast Ultrasound b) Plasma E2.

**Results:** Significant differences were between the median E2 levels among the various Child scores of the cases 74.3 pg/ml (17.2-159) pg/ml and that of the controls 9 pg/ml (9-19) pg/ml. $P < .001$; - Significant difference was between the median estrogen level among patients with C and D Breast densities 71.9 pg/ml (18.5-159) pg/ml was and that of patients with A and B 9 pg/ml (9-51.7) pg/ml. $P < .001$; - Significant positive linear correlation between cirrhosis and breast density. $p < .001$; -None of the cases showed malignancy.

**Conclusion:** Though the cases had more than a risk factor (age & breast density) apart from the existence of a possible pathogenic HCV mechanisms, there was no evidence supporting an association between HCV and breast cancer.

## RETROSPECTIVE ANALYSIS OF CLINICOEPIDEMIOLOGICAL FACTORS IN ENDOMETRIAL CANCER

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**Introduction:** Endometrial cancer is the most common female genital cancer in the developing world, with adenocarcinoma of the endometrium the most common type.

**Methods:** we retrospectively collected the clinical data of 104 patients treated at Ain Shams university hospital from January 2010 to December 2014. Demographic data, clinic-pathological factors, age, performance status (ECOG), comorbidities, risk factors, surgery, adjuvant treatment, metastatic treatment, treatment response and survival rates were collected.

**Results:** median age of the studied population was 61 years (range: 45-77), majority of our patients (86.5%) had good ECOG performance status (1), (57.6%) of the patients were presented to us with stage I disease, most common symptoms at presentation was abnormal vaginal bleeding in (96.15%) and the most common pathological subtype was endometrioid adenocarcinoma (88.4%). The median of overall survival (OS) of the recorded patients in the thesis is thirty six months in non- metastatic patients and fourteen months in metastatic patients. As regard adjuvant treatment fifty patients received Radiotherapy on whole pelvis till 50 Gy. Radiotherapy improved the OS and DFS (p=0.001). Twenty three patients received adjuvant Taxol/Carb with statistically significant improvement in OS (p=0.007).

**Conclusion:** In our study, age, risk factors (eg, DM, Hypertension), pathology, surgical staging, stage at presentation and adjuvant treatment (Rth, Cth<Taxol/Carb>) affect the OS, DFS & PFS with clinical significance.

## EXPRESSION OF IMMUNOMODULATOR PD-L1 AND FOXP3 IN SQUAMOUS CELL CARCINOMA OF CERVIX

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**Introduction:** Cervical cancer represents the third most common cancer in women with higher cancer related mortality in developing countries. Decrease in the immune response plays a role in expansion of tumors by retarded clearing of the malignant cells. Programmed death ligand 1 (PD L1) is a modulator of immune system. Once it binds to its ligands, it decreases the action of cytotoxic CD8 T cells in response to both viral and/or cancer cells. Fork head box protein 3(Foxp3) also inhibits the local immune reaction. To improve the prognosis of cervical cancer, novel immunotherapeutic schemes have to be settled.

**Material and Methods:** Archival paraffin embedded specimens of 31 cases of squamous carcinoma of cervix were examined by immunohistochemistry for FoxP3 and PD-L1 . Clinical data were abstracted from the reports of corresponding department.

**Results:** Among the 31 cases of squamous carcinoma of cervix, PDL1 expressed in of 16 (51.6%) and 17 (54.8%) cases of cancer cervix in tumor cells and infiltrating inflammatory cells, respectively. No significant correlation between PDL1 expression and clinicopathological characters of cancer cervix was found. Foxp3 were expressed in all cases of cervical cancer and their expressions were related to FIGO stage, tumor size, margin and lymph node metastasis ($p < 0.001$, $p = 0.021$, $p = 0.003$ and $p < 0.001$, respectively). There was no correlation between PD L1 and Fox3 expression. PDL1 expression in both tumor cells and lymphocytes was insignificantly correlated with patient's survival. In contrast, Foxp3 was associated with progressive disease and reduced overall survival ($p < 0.001$).

**Conclusion:** PD L1 which is a target of immunotherapy is expressed in both the carcinoma and infiltrating inflammatory cells in cervical SCC suggests that it is valuable to be investigated in these cases. Foxp3 is highly expressed in the cervical SCC, and represents an independent poor prognostic marker. No correlation between both markers indicating different pathways in their expression.

## OVERVIEW OF BREAST CANCER (DAMIETTA CANCER INSTITUTE EXPERIENCE 2006-2016)

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**Introduction and objective:** Breast cancer is the most common cause of cancer death among women worldwide. According to Egypt National Cancer Registry: Breast cancer is the most common cancer among women. Representing 15.4% of total cancer cases (38.8%) in women.

**Material and Method:** This is a retrospective study performed at Damietta Cancer Institute (DCI) between 2006 and 2016 and included 3928 cases aged 51.9 + 11.8 pathologically proved Breast Cancer. The data in this study are based mainly on computerized hospital cancer registry program (DCI) and patients' files. Among 4106 cases diagnosed as a breast cancer case, 178 cases were excluded from the study due to loss of data. In this study we investigate : Numbers of cases presented per year, Patient age, Breast cancer male : female ratio, cases presented by distant metastasis, Tumor Characteristic (Anatomic subsite/ Laterality) and Histologic Type

**Result:** Our patients tend to have different epidemiology and presenting with aggressive phenotypes. About 17% of breast cancer cases occur in women under 40 years of age while it is less than 7% in the world study. TUMOUTS are relatively advanced at presentation. About 15% of cases presented with stagr IV disease, while it is from 5% to 10% in the world study. The majority of tumours are invasive duct subtype. The profile of hormone receptors is positive for estrogen receptors and/or progesterone receptors In less than half of cases. There has been a dramatic shift in the surgical treatment of breast carcinoma over the last 10 years towards more conservative surgery.

**Conclusion:** It's not enough to cope with latest international guide line to treat our patient. It's must for cancer committees and physicians in Egypt to develop standards for their own institutions and facilitate any necessary adjustments to maximize conformance with those developed standards.

## HIGH RISK LESIONS: EXCISE OR FOLLOW UP?

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**Introduction:** High risk lesions are not malignant but are considered to have an increased lifetime risk for the development of breast cancer (e.g., atypical ductal hyperplasia, lobular neoplasm, radial sclerosing lesion, flat epithelial hyperplasia and papillary lesions). Controversy and lack of consensus exist in the management of these lesions. The aim of this study is to assess the upgrading rate of different histological types of high risk lesions to evaluate the necessity of surgical excision.

**Patients and methods:** this retrospective study was IRB approved and HIPAA compliant. All consecutive cases with tissue diagnosis of high risk lesions at their core needle biopsies (CNB) from 2010 to 2015 at university of Virginia were included. Type of mammographic and ultrasound findings, CNB guidance, needle gauge, and surgical excision results were tracked for each patient. The upgrading rate was calculated. Frequencies were compared by the McNemar test and the Pearson's Chi-square exact test.

**Results:** 166 cases with high risk lesions at their CNB met our study criteria. 101 had stereotactic- guided CNB while 65 had US-guided CNB. The rate of upgrading to malignancy at surgical excision is 30 cases (18%). 18 (60%) were DCIS, 9 (30%) IDC, 2 (6.7%) ILC, and 1 (3.3%) intracystic papillary carcinoma. Upgrading rate varies significantly according to the histological type of high risk lesion (30% of ADH, 13.7% of lobular neoplasia, 5.4% of papillomas, and 0% of radial scars) ($p<0.001$). There are no significant relations between the upgrading rate and biopsy guidance or needle gauge ($p= 0.470$ and 0.724) respectively.

**Conclusion:** the overall upgrading rate of high risk lesions at surgical excision is 18%, which is high enough to consider surgical excision. However, it varies significantly according to histological types, so single uniform management plan does not seem appropriate for all types of high-risk lesions. Management should be tailored for each individual case.

## PREOPERATIVE LOCALIZATION OF SENTINEL LYMPH NODE IN BREAST CANCER PATIENTS BY NOVEL COMPUTED TOMOGRAPHY-LYMPHOGRAPHY GUIDED TECHNIQUE; EARLY RESULTS

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**Introduction:** SLN detection in breast cancer patients is performed commonly intraoperative either using dye, radioisotope or both. (CT)–lymphography (LG) was suggested as an accurate method for preoperative SLN mapping. However, it was mainly used as a guidance for the blue dye or the radioisotope method not as an independent localization method. A question is raised about the possibility of accurate localization of the SLN detected by CTLG which offers a detection rate of 100% in many studies. We investigated the usage of sliver clip as well as charcoal as preoperative localization methods for the SLN detected by CTLG in breast cancer.

**Patients and methods:** This study was designed to be prospective randomized controlled clinical trial including 50 patients with node negative early breast cancer in OCMU (4/2017- 3/2019). We are now revealing the early results of the first 20 cases. The patients were randomized into two groups; SLN localized using CT guided injection of liquid charcoal suspended solution (first group) or by placing a 3 cm silver wire using spinal needle inside or around the LN (second group). For every patient, SLN biopsy will be performed using the traditional method with a blue dye. Then dual search for the SLN localized by both the novel & traditional method will be performed.

**Results:** Results will be collected as reagrd the matching between the SLN detected by both techiques. Identification rate, accuracy & feasibility will be reported for the new technique and the traditional method as well. The ongoing results collected are very promising as regard accuracy and feasibility of detection.

**Conclusion:** We suppose that this method can offer two main advantages over the traditional SLN intraoperative methods which are; saving operative time needed for the intraoperative procedure as well as solving the problem of the need for complex logistic preparations especially for the usage of radioisotope.

## PIM1 PROMOTES OVARIAN CANCER GROWTH AND THE WARBURG EFFECT VIA C-MYC-GLYCOLYSIS SIGNALING AXIS

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**Introduction:** Ovarian cancer (OC) is the second most common gynecologic malignancy, but its mortality ranks the highest in the world. Pim1, belongs to a group of constitutively activated serine/threonine kinases, has been reported in many types of cancer. Little is known about Pim1 in OC.

**Material and Methods:** The protein expression of Pim1 was verified from the human protein atlas (www.proteinatlas.org), as well as ovarian cancer cell lines, and its association with survival were then analyzed by bioinformatic analysis. CCK-8 assay and colony formation were used to measure cell proliferation. In order to evaluate the mechanism of Pim1 in HGSOC, Extracellular acidification rate (ECAR) and oxygen consumption rate (OCR) and Lactate analysis were performed to find that Pim1 maintains Warburg effect via c-Myc-glycolysis signaling axis. In Vivo subcutaneous xenograft inoculation was also performed to certified its role.

**Results:** Silencing/overexpressing of Pim1 suppressed/promoted OC cells proliferation in vitro. Pim1 significantly influenced glycolysis by OC cells and was associated with p-c-myc protein levels and subsequent c-myc regulated key enzymes (such as PGK1, LDHA) in the glycolytic pathway. Pim1-knockdown also inhibited ovarian tumor growth in vivo. Moreover, Pim1 inhibitor SMI4a exerted chemosensitizing effects on cisplatinum. Pim1 was also overexpressed in ovarian cancer and correlated with the poor overall survival of patients by bioinformatics analysis.

**Conclusions:** Together, these results suggest that Pim1 contributes to OC proliferation and glycolysis through p-c-myc axis, which may serve as a potential target for OC patients.

## LAUNCHING GUIDELINES FOR MANAGEMENT OF DOUBLE PRIMARY MALIGNANCY IN NASSER INSTITUTE CANCER CENTRE

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**Background:** although that there is evidence of increase incidence of double primary cancer cases, there is no international guidelines for treatment to be applied on these cases.

**Purpose:** to launch a local guidelines in for management of second primary malignancy in Nasser Institute cancer Centre

**Methods:** we have studied published literatures in Google scholar and PubMed form January 2007 until December 2017, including case reports, prospective and retrospective studies for double primary cancer cases, and also we studied data base files of Nasser Institute Hospital for Research and treatment for double primary cases, then we compared management methods and results of treatment of all cases with National Comprehensive Cancer Network guidelines for each tumour type.

**Results: For diagnosis** of second primary, publications highlighted the importance of biopsy and IHC of second primary to confirm its diagnosis and accordingly, double primary cancer cases can be divided in to: 1- **Synchronous malignancies** were second cancer have been occurring either simultaneously, or within 6 months after the first malignancy and 2- **Metachronous malignancies** were secondary cancer that have developed after 6 months, or even more than that from the first malignancy.

There was no published clinical trials **treatment** of malignancy of double primary, and for this reason, any applied treatment will be based mainly on case report evidence.

**Patients on adjuvant therapy for first primary:** should continue adjuvant therapy as long as it's safe.

**Patient who ended adjuvant therapy for their first primary** before diagnosis of second primary, were treated by applying international guidelines for second primary.

Patients who had **two active malignancies (synchronous type)** were bad prognosis, and treated as recommended by tumour board trying to apply international guidelines for treatment of each cancer, and/or give recommendations that can treat both active primaries.

Close **follow up** is needed with new biopsy for each new lesion.

**Conclusion:** at present, guidelines for treatment of double primary cancer cases will be based mainly on case reports, raising the need of international prospective clinical trial for getting more evidence based guideline.

## IMMUNOHISTOCHEMICAL EXPRESSION OF GLUT-1 IN EPITHELIAL OVARIAN TUMORS:CORRELATION WITH THE CLINICOPATHOLOGICAL FACTORS AND TUMOR PROLIFERATIVE MARKER PCNA

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**Introduction and objectives:** Ovarian carcinomas are frequently diagnosed at advanced-stage due to lack of distinct symptoms and reliable procedure for early detection. The applying of immunohistochemistry has become an important tool improving the prognosis of patients with ovarian carcinomas. we assess the expression of Glut-1 in epithelial ovarian tumors and study its correlation with PCNA to detect their usefulness in the diagnosis and prognosis of such tumors.

**Material and Methods:** Glut-1 immunoexpression was analyzed and correlated with PCNA in 45 epithelial ovarian tumors (7 benign, 10 borderline and 28 malignant tumors).

**Results:** Glut-1 was expressed in 80% and 92.85% of the studied borderline and invasive carcinomas respectively, but not expressed in any benign tumors. These differences in Glut-1 expression among the benign, borderline and malignant cases, were statistically significant (p= 0.000). Analysis of Glut-1 immunoexpression with the clinicopathological criteria of ovarian carcinomas revealed that Glut-1 expression is more significantly expressed in high grade carcinoma and in tumors with an advanced FIGO stage (p=0.043 and p=0.005 respectively).Glut-1 was more significantly expressed in lymph node metastases positive group and in those with intraperitoneal implants (p=0.011 and 0.016 respectively).There was a strong positive significant correlation between Glut-1 and PCNA among the studied 45 ovarian tumors (Spearman correlation (r) = 0.603, p value= 0.000).

**Conclusion:** Glut-1 can increase the diagnostic accuracy of ovarian tumors by help in differentiating between benign, borderline and malignant tumors. Glut-1 correlated with poor prognostic factors and can be used with PCNA as prognostic markers for epithelial ovarian tumors.

## COMPARATIVE ANALYSIS OF THE UTILITY OF GATA-3 OPPOSED TO GCDFP-15 IN THE DIAGNOSIS OF METASTATIC BREAST CARCINOMAS AND DIVERSE MOLECULAR SUBTYPES

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**Introduction:** Triple negative breast carcinomas and around half of metastatic breast carcinomas (BC) are negative for estrogen receptor (ER) and the frequently used breast-specific immunomarker gross cystic disease fluid protein 15 (GCDFP-15). Recently, GATA-3 has emerged as a sensitive and a relatively specific immunomarker for breast and urothelial carcinomas. However, limited studies analyzed GATA-3 expression in various histomorphologic and molecular subtypes, specifically the triple-negative BC.

**Aim of the study:** to compare the utility of GATA-3 versus GCDFP-15 in diagnosing metastatic BC & diverse molecular subtypes of BC.

**Material and Methods:** Sixty- three cases of primary BC and metastatic BC are immunohistochemically stained with GATA 3 and GCDFP-15. Primary BCs are classified in accordance to their hormonal receptors profile into: ER (luminal) positive, Her-2 positive and triple-negative molecular subtypes.

**Results:** GATA-3 & GCDFP-15 expression has been detected in 90.4% & 47.6% of the studied cases, respectively. In primary BC, merely GATA-3 expression has significantly varied in the different molecular subtypes. GATA-3 is expressed in all (luminal) ER positive, 76.9% of Her 2 positive and 82.3% of triple negative molecular subtypes. GATA 3 has shown 100% and 82.4% sensitivity for diagnosis of metastatic breast carcinoma and triple negative breast cancer, respectively. However, the specificity of GCDFP-15 is superior to GATA-3 with values 60.5%vs 14% in metastatic breast carcinoma and 50% vs 11.5% in triple negative BC.

**Conclusions:** GATA-3 is more sensitive than GCDFP-15 in diagnosing metastatic BC precisely while encountering ER-negative BC. However, GATA-3 lacks the specificity of GCDFP-15.

## PHYLLODES TUMORS OF THE BREAST; REVIEW OF 99 CASES IN 10 YEARS

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**Background:** The frequency of mesenchymal breast tumors is very low, being represented mostly by tumors with biphasic proliferation (phyllodes tumors) and less by other types of non-epithelial tumors.

**Objective:** to review the Management of phyllodes tumors of the breast in the NCI Cairo university during a period of 10 years (2000 till 2010).

**Material and Methods:** retrospective study including 99 patients who diagnosed and treated with phyllodes tumors of the breast between (2000 to 2010).Data were collected from the biostatistics and cancer epidemiology department.

**Results:** Out of 99 patients; 51 (51.5%) were benign and 32 (32.3%) were borderline and 16 (16%) were malignant; the median age of the study population was 45.5 years (range 18_71years).The main radiological tool of diagnosis was breast US and mammography 100% .Preoperative fine needle aspiration (FNA) was performed in 12(37.5%) cases for cytodiagnosis but true cut biopsy was done in 87 (87%) cases. Wide local excision was done in 86%, wide local excision with axillary evacuation was done in 1% only, simple mastectomy was done in 9.3% and modified radical mastectomy was done only in 3% of all cases.

**Conclusion:** different surgical modalities are considered the main line for management of phyllodes breast tumors. Local recurrence can be avoided with wide local excision from the first surgery. Axillary LN dissection is not a role in management of breast PT.

**Keywords:** phyllodes tumor (PT), breast, fine needle aspiration (FNA).

## PREDICTION OF TRASTUZUMAB-INDUCED CARDIOTOXICITY IN BREAST CANCER PATIENTS RECEIVING ANTHRACYCLINE BASED CHEMOTHERAPY

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**Background:** adjuvant trastuzumab improved overall survival and reduced the risk for disease recurrence in women with breast cancers, Because of its potential cardiotoxicity, careful monitoring of left ventricular (LV) function during treatment is required

**AIM:** This study investigates, whether myocardial strain imaging and level of N-terminal pro- brain natriuretic peptide (NT-pro BNP) obtained early in the course of the treatment of breast cancer patients could predict subsequent reduction in LVEF.

**Methods:** a prospective single arm study included 61 Patients received AC (Doxorubcin) for 4 cycles, followed Trastuzumab, clinical, conventional echocardiographic parameters, myocardial strain imaging [global longitudinal peak systolic strain (GLS), radial and circumferential systolic strain] and level of NTpro- BNP were measured at baseline, after 3, 6, 9 and 12 months of trastuzumab therapy.

**Results:** of 61 patients, 18 patients (29.5%) developed trastuzumab induced cardiomyopathy (CM) at 6 and 9 months of therapy (LVEF declines ≤ 10%) no significant difference between CM group and group without CM as regard age and cardiac risk factors, GLS and radial strain significantly decreased in CM group at 3 months of trastuzumab treatment, the value of GLS at 3 months was the strongest predictors of cardiotoxicity its area under the curve (AUC,0.98) with an optimal cut off for GLS (-18%) having 92.5% sensitivity and 83% specificity. peak radial strain and peak circumferential systolic strain showed that the values of these parameters at 3 months predict the reduction in EF at subsequent months. Level of NT-pro BNP did not changes significantly in CM group during therapy.

**Conclusion:** myocardial strain imaging able to predict pre – clinical changes in LV systolic function and GLS is an independent early predictor of subsequent reduction in EF in breast cancer patients treated with trastuzumab.

## PROGNOSTIC SIGNIFICANCE OF TRANSFORMING GROWTH FACTOR B RECEPTOR II IN CLINICAL STAGE III BREAST CANCER PATIENTS

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**Background:** The transforming growth factor–β (TGFβ) plays a dual role in breast cancer, acting as a tumor suppressor in early carcinomas while promoting tumor metastasis in more advanced breast carcinoma. As a result, the prognostic role of TGFβ and its signaling components in breast cancer remains unclear

**Objectives:** to investigate the relationship between TβRII [type II TGFβ (transforming growth factor β) receptor] expression and clinic-pathological characteristics, and to evaluate the prognostic significance of TβRII expression in advanced breast cancer (Clinical stage III).

**Methods:** Biopsy from the primary tumor obtained from all patients before receiving any therapy. The expression of TβRII assessed by immunohistochemistry. They underwent surgery, (neo) adjuvant therapy according to standard of care protocols.

**Results:** Of the 30 patients who enrolled into this study, 20 cases were TβRII positive and 10 cases were negative. The TβRII expression rate was significantly increased in patients with N2 and N3 lymph node metastasis compared to those with N0 and N1 lymph node metastasis (60 % vs 40%; P = 0.038). After a median follow up of 42.3 months. Survival analysis demonstrated that TβRII was associated with poor DFS (P = 0.003). Patients with high TβRII expression showed poorer disease-free survival (DFS) compared to those with low expression (HR=7.215; P=0.011) by cox regression analysis and it was an independent factor for predicting the poor outcome for breast cancer patients.

**Conclusions:** TβRII expression was associated with high stage lymph node metastasis, and poorer DFS in patients with clinical stage III breast cancer. TβRII is an independent, highly significant prognostic indicator for disease free survival in clinical stage III breast cancer.

**Keywords:** transforming growth factor–β, Breast cancer.

## ALL-ORAL COMBINATION OF LAPATINIB AND LETROZOLE AS FIRST-LINE THERAPY IN PATIENTS WITH HORMONE RECEPTOR–POSITIVE HER2-POSITIVE METASTATIC BREAST CANCER- A PHASE II STUDY

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**Purpose:** The aim of this study is to investigate efficacy and tolerability of the combination of letrozole plus lapatinib (LL) as first-Line therapyin hormone receptor–positive (HR positive), HER-2 positive metastatic breast cancer (MBC).

**Patients and Methods:** Between January 2013 and January 2015, 42 postmenopausal patients with pathologically proven HR –positive HER2+ –positive MBC, were included. Ttirty two patients (76.19%) progressed after prior adjuvant hormonal treatment and 10 patients (23.81%) were hormonal -naïve for MBC. Patients received lapatinib 1500 mg once daily every morning continuously and letrozole 2.5 mg once daily continuously. Twenty four patients (57.1%) initially treated by trastuzumab-based regimens in either adjuvant or neoadjuvant setting of disease. No patients had received prior lapatinib and/or letrozole. Endpoints were response rate (RR), progression free survival (PFS), overall survival (OS) and toxicity.

**Results:** The overall response rate (ORR) was 28.6% (12/42) and all were partial response. Median PFS was 9months. For patients received prior adjuvant hormonal treatment and hormonal -naïve patients the median PFS was 9.00 months and 13.00 months respectively. Median OS was 33 months. Treatment-related adverse effects were tolerable. Grade 3–4 toxicities were diarrhea (9.5%), nausea/vomiting(4.7%),and rash(4.7%).

**Conclusion:** The oral combination of LL well-tolerated and effective treatment in patients with HR –positive HER2+ –positive MBC.

**Key words:** Hormone receptor–positive, HER2+ –positive breast cancer, metastatic breast cancer, letrozole, lapatinib.

## NOVEL MUTATIONS IN THE BRCA2 GENE IN YEMENI WOMEN WITH BREAST CANCER

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**Background:** Breast cancer is a major cause of death among women worldwide. In Yemen, it the most commonly diagnosed cancer among women, an average of breast incidence rate in Yemen was 20.9 (1261 cases). Among many risk factors of BC, mutations in BRCA2 gene were found to be the primary cause in 5–10% of cases. The etiology of (BC) in Yemen is scarcely investigated. The study aimed to describe the pattern of mutations including single nucleotide polymorphisms and variants of the *BRCA2* (exon11) genes among Yemeni women patients diagnosed with BC.

**Methods:** In this study DNA was extracted from tissue blocks of the patients who attended oncology center-Sanaa city and undergo breast biopsy, from May 2015 to May 2016. One hundred and fifty patients were enrolled in this study; one hundred samples were breast cancer and fifty were benign breast lesions and served as control. Polymerase Chain Reaction (PCR) using primers that target regions from 3281 to 3731 (A) and 4967 to 5673 (B) of BRCA 2 exon 11 and Sanger sequencing were performed for all samples. The study was approved by Ethics Review Committee Board of A1 Neelain University.

**Results and dissections:** Of the 150 suspected cases, 100 proved to be breast cancer as case and fifty to be breast benign lesions as controls. The age of the patient ranged from 22 to 75 years, the median age of cases was 46.2 years and 28.3 years for controls In 100 breast cancer cases nineteen mutations and one in 50 were detected in BRCA2 within two regions were selected position A & B and one variants was detected in all fifty breast benign lesions.

From nineteen mutations were detected 17 mutations were pathological mutations and 2 were silent mutations and the one pathological mutation in control. The pathological mutations frequency 18% in BRCA2 were detected in Yemeni breast cancer patients more than that reported in world figures (5-10%).

**Conclusion:** This study detected a novel mutations in Yemeni patients diagnosed with breast cancer. Further work is needed to demonstrate its usefulness in screening of BC.

**Keywords:** *BRCA2*, FRAME SHIFT, novel mutation, silent mutations, Breast cancer, Yemeni patients.

## LOCO REGIONAL CONTROL AFTER BREAST CONSERVING SURGERY FOR T1 AND T2 LESIONS: A FIVE YEAR RETROSPECTIVE STUDY AT THE NATIONAL CANCER INSTITUTE

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**Introduction and objective:** Breast conservation therapy (BCT) is currently the treatment of choice for women with early-stage breast cancer (stage I or II). This retrospective study was done to assess the significant factors affecting loco-regional recurrence (LRR) and the overall survival in female patients who underwent breast BCS.

**Material and method:** Between January 2006 and December 2010, 223 patients were diagnosed by T1 or T2 breast cancer. By studying their medical records, 187 patients met the inclusion criteria. Different prognostic factors were thoroughly assessed.

**Results:** LRR occurred in 21 patients (11%) and 27 patients (14%) died during follow-up. The median of overall survival (OS) was 70 month. The median of LR free survival was 60 months. Delaying surgery more than one month after diagnosis worsened OS (*p 0.024*). The presence of positive lymph nodes lowered the OS and higher incidence of LRR (p *0.002 and p 0.004 respectively*). The number of positive lymph nodes (≥4) negatively affected the overall OS (*p 0.001*). Omitting adjuvant hormonal therapy had negative impact on LRFS (*p 0.005*). On multivariate analysis, positivity of axillary lymph nodes (HR: 3.3, 95% CI: 1.4-7.9) and time from diagnosis till operation > 1 month (HR: 2.7, 95% CI: 1.0-7.1) had worse OS *(p=0.007, 0.049 respectively*). On multivariate analysis, positivity of axillary lymph nodes (HR: 4.5, 95% CI: 1.6-12.4) and not receiving hormonal treatment (HR: 3.7, 95% CI: 1.6-8.9) had worse LRFS (*p=0.003, 0.003 respectively*).

**Conclusion:** LRR was mainly influenced by the lymph node status and omitting hormonal therapy. The OS had an inverse relation with the number of positive axillary lymph nodes and the delay of surgery more than one month after diagnosis.

## EXPRESSION OF P450 AROMATASE IN GRANULOSA CELL TUMORS OF THE OVARY

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**Background:** Granulosa cell tumors are a neoplasm occurring mostly in the ovary which often produces estradiol. Granulosa cell tumors are representative of estrogenic ovarian tumors. Aromatase is an enzyme that catalyzes the desaturation (aromatization) of the ring A of C19 androgens and converts them to C18 estrogens.

**Results:** Among the 20 granulosa cell tumors examined, 14 were associated with estrogenic function, including endometrial hyperplasia and/or significant elevationof serum E2, whereas 6 were not. Aromatase was detected in 11 of the 14 estrogenic cases, whereas it was not detected in 5 of the 6 nonestrogenic cases. In aromatase-positive estrogenic cases, there was no correlation between the pattern of aromatase-positive cells and estrogenic function.

**Conclusion:** The expression of P450 aromatase corresponds to specific cell morphology in sex cord-stromal tumors, including recurrent tumors. Aromatase status in granulosa cell tumors provides helpful information on whether serum estradiol could be a marker for recurrence.

**Keywords:** Granulosa cell tumors, Ovary, P450 aromatase, Estrogen.

## SYNDECAN-1 EXPRESSION ON BREAST CANCER CELL PROMOTING M2 MACROPHAGES POLARIZATION

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**Introduction:** The transmembrane heparan sulfate proteoglycan Syndecan-1expression induced in a variety of cell types during development and tumor progression and plays an essential role in regulation, recruitment and activation of monocytes in tumor microenvironment. A growing body of evidence indicates tumor associated macrophages (TAMs) are classified into major phenotypes, tumor inhibiting M1 and tumor promoting M2. The role of syndecan-1 in macrophage polarization is poorly studied.

**Materials and Methods:** In the present study, Sydecan-1 expression was silenced in MDA-MB-231 and SUM-149 cells using siRNA approach. The transfected cells were used in direct and indirect coculture with breast cancer patients – derived monocytes and U937 cells to test their effect on macrophage polarization. The expression levels of markers of the M1 state such as IL-1 beta, as well as those of markers of M2 activation, such as IL-10 were measured by RT-qPCR. Furthermore, the M1 marker HLA-DR and the M2 markers CD163 and CD206 were assessed by flow cytometry.

**Results:** Our findings indicate that the Syndecan-1 silenced cells promoted macrophage polarization M1 by upregulating expression of IL-1 beta by 32% and suppressed M2 by suppression of IL-10 expression by 28% in both coculture conditions-Relative to controls, CD206 and CD163 markers were downregulation and HLA-DR marker was upregulated upon coculture with Syndecan-1 silenced cells.

**Conclusion:** Overall, these findings highlight the potential role played by Syndecan-1 in promoting M2 polarization, thus Syndecan-1 may emerge as therapeutic target for breast cancer.

## PREDICTIVE SIGNIFICANCE OF STROMAL ASSOCIATED LYMPHOCYTES IN RESPONSE TO NEOADJUVANT CHEMOTHERAPY IN BREAST CANCER"

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**Abstract:**

**Objectives:** in this work we aimed to assess whether the high stromal associated lymphocytes and their subtypes in pretreatment core biopsies from patients with invasive breast carcinoma have a predictive role in pathologic response to neoadjuvant chemotherapy

**Background:** Tumor infiltrating lymphocytes including stromal associated lymphocytes in breast cancer are considered a form of the host immune response to malignancy. Several studies suggested that tumor-infiltrating lymphocytes could predict better response to neoadjuvant chemotherapy but their roles in predicting pathologic complete response rateafter neoadjuvant chemotherapy still needs further evaluation

**Material & Methods:** Stromal associated lymphocyteswere evaluated in 100 pretreatment core biopsies from primary breast cancer patients eligible for neoadjuvant chemotherapy. Cases were defined as lymphocyte-rich if the percentage of lymphocytes were more than 50% and also the lymphocytes were evaluated for CD20, CD3, CD8, and CD4. Type of pathological response to neoadjuvant chemotherapy was determined in post therapy surgical specimens of the same patients, and, we correlated between type of response to stromal associated lymphocytes and their subtypes.

**Results:** Complete pathologic response was detected in 22 cases (22%) of breast cancer patients, partial pathologic response in 54cases (54%), no pathologic response in 24 cases (24%) of patients. Significant association between percentage of stromal associated lymphocytes and achievement of pathologic complete response rate ($p$= 0.006). Also, high stromal associated lymphocytes are significantly associated with advanced histological grade ($p$=0.004), Ki-67 ($p$=0.028), negative ER state ($p$=0.015)

**Conclusion:** High stromal associated lymphocyte and highpercentage of CD8+ T-cells in stromal associated lymphocytes could be reliable predictors for pathologic complete response rate after neoadjuvant chemotherapy

**Keywords:** Breast cancer, Neoadjuvant chemotherapy (NACT), stromal associated lymphocytes, tumor-infiltrating lymphocytes (TILs)

## OUTCOME OF NODE NEGATIVE BREAST CANCER IN EGYPTIAN PATIENTS: CORRELATION WITH MOLECULAR CLASSIFICATION. A SINGLE INSTITUTE EXPERIENCE

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**Introduction and Aim:** Breast cancer is newly classified based on immunohistochemistry (IHC) for hormone receptors (HR), human epidermal growth factor receptor (HER2) and Ki-67. This classification reflected on patients' prognosis and management. It poses a challenge on the use of adjuvant therapy in early stages of breast cancer with absence of axillary lymph node involvement. We conducted this study to determine the outcome of lymph node negative breast cancer in patients at the National Cancer Institute (NCI), Cairo University.

**Material and Methods:** The study was conducted retrospectively on tumor specimens from females diagnosed with lymph node negative invasive breast cancer, obtained from the archives of the NCI, Cairo from January 2007 till December 2010. Patients were classified according to IHC panel (HR, HER2, and Ki-67) into molecular subsets. Tumors were further grouped by size and adjuvant therapy received.

**Results:** 113 patients were followed for a median period of 46.9 months (range, 2.7–91.3). Cases were categorized into luminal A (31%), luminal B (35.4%), luminal HER2/neu (9.7%), HER2/neu-enriched (12.4%) and TNBC (11.5%). Most cases (66%) received adjuvant therapy (62.9% of Luminal A, 60.0% of Luminal B, 63.6 of luminal HER2/neu, 78.6% of Her2-enriched, and 85% of TNBC), the difference was statistically non-significant (*P-value 0.3*). DFS was not significantly different (*P value 0.7*) among different breast subtypes or among tumors of large size (*P value 0.3*). TNBC subtype had the worst 5-years OS (49.5%), however the only significantly difference was the superior OS for Her2-negative over Her2-positive cases (*P-value 0.02*).

**Conclusions:** Node-negative breast cancer generally have a good outcome. No substantial difference in survival was evident among different molecular subtypes. Other biomarkers may identify those node-negative patients with favorable prognosis.

## EFFECT OF WIN-55,212-2 ON TUMOR GROWTH AND CANNABINOID CB1 AND CB2 RECEPTORS EXPRESSION IN NMU-INDUCED RAT MAMMARY TUMOR

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**Introduction and Objectives:** Breast cancer is one of the most common and lethal cancers among women worldwide. Recently, the antitumorigenic effects of cannabinoids, the active component of marijuana, have emerged as an exciting field in cancer research. The aim of the present study was to evaluate the effect of mixed CB1/CB2 synthetic cannabinoid agonist WIN-55,212-2 on tumor development and cannabinoid receptors (CB1 and CB2) expression in N-methyl-N-nitrosourea (NMU)-induced mammary carcinogenesis in female rats.

**Materials and Methods:** Seventy-five rats were divided into five groups: control group, NMU group (administrated with NMU), pre-treated group (received WIN-55-212-2 two weeks before NMU), co-treated group (received WIN-55-212-2 at the same week of NMU), post-treated group (received WIN-55-212-2 after the first tumor appearance). CB1 and CB2 receptors expressions in tumors and normal mammary glands were assessed by immunohistochemical analysis. Anticancer activities of WIN-55,212-2 were studied by monitoring carcinogenesis parameters (latency period and tumor incidence, frequency, volume and weight). Some hormonal and biochemical parameters were also determined.

**Results:** Administration of WIN-55,212-2 significantly decreased tumor incidence, tumor frequency per animal, average tumor volume, and lengthened the latency period compared to NMU group. A histopathological analysis of mammary tumors revealed a shift from poorly-differentiated IDCs in NMU group to well-differentiated and benign tumors in WIN-55,212-2-treated groups. Enhanced CB1 and CB2 expression was significantly observed in malignant compared to benign and normal breast tissues. However, the administration of WIN-55,212-2 showed higher CB2R expression than CB1R, especially in well-differentiated and benign breast lesions. WIN-55,212-2 also reduced serum concentrations of prolactin, estradiol, progesterone, ALT, AST, urea and creatinine compared to NMU group.

**Conclusion:** This study suggests the marked chemopreventive and antineoplastic activity of WIN-55,212-2 against NMU-induced mammary carcinogenesis and the possible role of cannabinoid receptors in the pathophysiology of breast carcinoma.

**Keywords:** Breast cancer; Cannabinoids, WIN-55,212-2; Cannabinoid Receptors; CB1; CB2; NMU; Mammary carcinogenesis; Antitumorigenic.

## PROSPECTIVE PILOT STUDY OF TRASTUZUMAB – PERTUZUMAB – PACLITAXEL – CARBOPLATIN (HERPETAC) IN THE TREATMENT OF HER2+ METASTATIC BREAST CANCER

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**Introduction and objectives:** Breast cancer with positive HER-2neu is an aggressive disease with poor prognosis. The addition of pertuzumab to trastuzumab and docetaxel significantly improved survival in metastatic setting, but an area of investigation is whether other chemotherapies could provide same efficacy. In this prospective, open-label, non-randomized pilot study, we aimed at evaluating the efficacy and safety of trastuzumab – pertuzumab – paclitaxel – carboplatin combination regimen.

**Patients and Methods:** Between June 2016 and October 2017, metastatic breast cancer patients received trastuzumab 6 mg/m$^2$ Q3W, pertuzumab 840 mg in the 1$^{st}$ cycle followed by 420 mg in subsequent cycles Q3W with paclitaxel 60 mg/m$^2$ and carboplatin AUC 2 weekly non-stop; the patients continued treatment for 6 cycles and patients achieved response continued trastuzunmab - perjeta alone Q3W.

**Results:** Twenty patients were included and their median age was 40 (range 27-74). Twelve patients were premenopausal (60%). Estrogen and Progesterone receptors were positive in 75% and 65% respectively. The median disease free survival (DFS) before recruitment in the study was 24 months (95% CI, SE 11.547). Fourteen patients (70%) received previously Trastuzumab in the adjuvant setting. The number of metastatic sites at time of inclusion ranged from 1-3 sites, 35%, 35% and 30% respectively. CNS metastasis was present in 4 patients only (20%). After a median follow up period of 8 months (range 3-18 months), the median PFS was not reached and the 1-year PFS rate was 64.3%. Seven patients (35%) achieved complete response (CR), 5 patients achieved partial response (25%) with overall response rate (ORR) 60% in addition to one patient remained stable. Clinical benefit rate (CBR) was 65%. The 12 patients who achieved response continued maintenance trastuzumab - pertuzumab for a median number of cycles 10 (range 2-18). One patient only developed grade III neutropenia. Seven patients (35%) reported no toxicity and 65% developed grade I-II toxicity; 25% neuropathy, 15% vomiting and neutropenia, 10% anorexia and fatigue and 5% nausea and weight loss.

**Conclusion:** The HerPeTaC protocol was effective with comparable response rate and progression free survival rates as the standard Trastuzumab – Pertuzumab – Docetaxel protocol but with acceptable toxicity.

**Keywords:** HER2+, Trastuzumab, Pertuzumab, Breast cancer.

## NAB – PACLITAXEL WEEKLY SCHEDULE IN METASTATIC BREAST CANCER, DUBAI HOSPITAL

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**Aim of The Study:** On January 7, 2005, the U.S. Food and Drug Administration approved paclitaxel protein-bound particles 260mg/me every 3 weeks for injectable suspension (ABRAXAN, *nab*- Paclitaxel), albumin-bound for treatment of breast cancer after failure of combination chemotherapy for metastatic disease or relapse within six months of adjuvanthttps://www.cancer.gov/dictionary?expand=a - adjuvant therapy chemotherapy. Nanoparticle paclitaxel is also called paclitaxel albumin-stabilized nanoparticle formulation.

This retrospective study was done to analyse the efficacy, toxicity and survival of weekly schedule of Abraxan in metastatic breast cancer patient who attended oncology department at Dubai hospital in the period between May 2014 and June 2017.

**Patient and methods:** The medical records of twenty-three patients with metastatic breast cancer who attended oncology department at Dubai Hospital between May 2014 and June 2017 and received Abraxan chemotherapy in the first or subsequent treatments lines were reviewed after getting the ethic committee approval. Demographic information, disease characteristics, response rates, toxicity and survival data were collected. all the patient received weekly Abraxan 100 mg/m2 - 125mg/m2 on D1, D8, & D15 of 28-day cycles (No. 23 patients).

**Results:** Weekly Abraxan scheduling is a well tolerable chemotherapy. Abraxan demonstrated an overall response rates of 65.2% among patient with metastatic breast cancer. The median time to disease progression was 20 weeks (95% confidence interval 17.45 – 22.54). No hypersensitivity reaction observed among the patient who received Abraxan. The overall toxicity observed in 15 out of 23 patients (65.2%). Grade three or four toxicity observed in 6 patients (26.1%).; one patient developed grade ¾ hematologic toxicity but 7 out of 23 patients developed grade ¾ sensory neuropathy.

**Conclusions:** *Nap* -paclitaxel (Abraxan) in weekly schedule showed significant high response rates with manageable toxicities. High grade ¾ sensory neuropathy could be related to higher cumulative total dose.

## GRANULOMATOUS MASTITIS DILEMMA: OUR INSTITUTIONAL EXPERIENCE

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**Background:** Idiopathic granulomatous mastitis (IGM) is an uncommon chronic, non caseating inflammatory lesion in the breast with obscure etiology usually presents with multiple masses, abscesses and sinus formation. Treatments include surgical excision, systemic steroids, antibiotics, drainage or even expectant treatment. To date, there is no agreement about the most standard treatment regimen. In our study, we aimed to describe the clinical and pathological characteristics of 23 patients admitted to our clinic with definitive diagnosis of IGM and different treatment modalities.

**Patients and Methods:** We performed a retrospective chart review of patients with granulomatous lobular mastitis treated from May 2014 to May 2017. Findings of clinical, radiological, and pathological examinations were collected and analyzed. Therapeutic modalities and patients' outcome were presented.

**Results:** The majority of patients were at the reproductive period with history of lactation. (15) patients presented with mass, (5) presented with abscess. (3) with skin changes. USG was done for all patients. MM was done for 17 patients. MRI was performed in 6 patients. Initial treatments included wide excision (12), excision after 3 months course of steroid (3). drainage with adjuvant steroids (4), antibiotic followed by excision (3). Recurrence was seen in three patients.

**Conclusion:** IGLM is a rare inflammatory breast disease found in young women of reproductive age. Usual presentation is painful, irregular mass which mimics carcinoma. Neither clinical nor radiological investigation are sufficient for diagnosis. Histopathological examination plays the main role. Treatment is controversial and should be tailored according to disease severity, extent symptom and also patient preference.

## SQUAMOUS CELL CARCINOMA OF THE BREAST; A RETROSPECTIVE STUDY

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**Abstract**

**Background:** Squamous cell carcinoma of the breast is an extremely rare tumor with vague natural behavior and treatment. The purpose was to identify the clinicopathologic features and treatment results of this rare type of breast cancer.

**Material and methods:** The medical files of patients with squamous cell carcinoma of the breast presented to Alexandria Main University Hospital during the period from January 1990 to January 2010 were retrospectively reviewed, regarding clinicopathologic characteristics and treatment outcome and analyzed.

**Results:** Seventeen patients were included in this analysis. The median age was 50 years. All patients presented by breast mass. The majority of tumors (88.2%) were negative for hormone receptors. Two thirds of patients had early T-stage. All patients underwent surgery in our center. Adjuvant Tamoxifen was given for two patients. Twelve patients (70.6%) received different adjuvant chemotherapy protocols and eight patients received radiotherapy.

The median disease-free survival was 24 months and the median overall survival was 40 months. Patients received adjuvant chemotherapy had significantly better disease-free survival ($p = 0.014$) and overall survival ($p = 0.019$) compared to those treated without chemotherapy. Radiotherapy had no significant impact on either disease-free survival or overall survival.

**Conclusions:** Squamous cell carcinoma of the breast is very aggressive tumor and adjuvant chemotherapy should be strongly considered.

**Keywords:** Breast cancer, Prognosis, Squamous.